

about five amino acids comprises at least about 20 amino acids of SEQ ID NO: 4.

- F1
82. (New) The purified antibody of claim 80, wherein the polypeptide comprising at least about five amino acids comprises SEQ ID NO: 4.
- Q2
83. (New) The purified antibody of any of claims 80-82, wherein the antibody is a polyclonal antibody.
84. (New) The purified antibody of any of claims 80-82, wherein the antibody is a monoclonal antibody.

ADD F1

RESPONSE

Pending claims

Claims 4-6, 29, 33 and 37-60 are pending. Upon entry of this Amendment and Response, new claims 61-84 are presented for consideration.

Claims are canceled herein solely to expedite prosecution of the instant application and without prejudice to pursuing these claims in continuing and other related applications. No new matter is added by this amendment. Support for the newly added claims are found throughout the specification, in the claims as originally presented and in the Figures. In particular, attention is directed to the present application at page 38, page 41, lines 3-8, page 40, line 25 through page 41, line 1, and page 57, lines 5-7. Support for antibodies which do not cross-react with non-LAT ZAP 70 or non-LAT Syk substrates may be found at least at page 38, lines 9-12. Support for antibodies that are generated against a polypeptide of at least about 5 amino acids of the amino acid sequence of SEQ ID NO. 4 may be found at page 44, lines 6-9, for example. Support for antibodies directed against the cytosolic tail of LAT may be found at least at page 40, line 25 through page 41, line 1. Support for antibodies generated against polypeptides comprising amino

acids 31 to 233 of LAT may be found at least at page 57, lines 5-7. This sequence represents the sequence used as an immunogen to generate the antibodies disclosed in Applicants' Examples.

Applicants thank the Examiner for his helpful comments during the telephonic interview of October 24, 2002. The newly added claims provided with this filing are made to address the issues raised by the Examiner during the interview. It is believed that the new claims place the application in condition for allowance.

Objection to the Specification

The Examiner has objected to the Specification and states that "Schematic A" provided on page 37 should be removed and provided in the form of a Figure.

Applicants provided with their previous Amendment and Response to Final Rejection new Figures 17 and 18, to provide formal drawings corresponding to Schematic A and B respectively and have amended the Brief Description of the Drawings and the specification, as appropriate, to reflect this change.

Applicants thank the Examiner for approving the drawings submitted with Applicants' previous Response filed October 8, 2002, as indicated by the Advisory Action mailed October 28, 2002. Applicants respectfully request entry of the amendments to the Specification to describe the newly added Figures.

Rejection of Claims 4, 6, 29 and 37 Under 35 U.S.C. § 102(b) (Buday)

Claims 4, 6, 29 and 37 are rejected under 35 U.S.C. § 102(b) as being anticipated by Buday, et al., *The Journal of Biological Chemistry* 269: 9019-9023, 1994 ("Buday").

The Examiner asserts that Buday teaches an antibody specific for phosphotyrosine which is a portion of SEQ ID NO. 4 and therefore that the antibody of Buday would bind to SEQ ID NO: 4.

Applicants respectfully traverse the rejection as it would be applied to the newly added claims. Newly added claims 61-69 recite antibodies that specifically bind to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4 and do not cross-react with non-LAT ZAP 70 or non-LAT Syk substrates. Claims 70-84 recite that the antibodies are generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4 and that specifically bind to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4.

Unlike the antibodies of the instant claims, Buday's antibody *would* cross react with non-LAT ZAP 70 or non-LAT Syk substrates, since it would react non-specifically with *any* polypeptides comprising a phosphotyrosine group. Therefore Buday neither teaches nor suggests the antibodies of claims 61-69.

With respect to claims 70-84, Buday's antibody is *not* generated against a portion of a LAT polypeptide comprising *at least about five amino acids of SEQ ID NO. 4*. This element of claims 70-84 must be given weight because the way in which the claimed antibodies are made *does* impact the structure and properties of the antibodies. The antigen-binding site of the claimed antibodies must recognize at least 5 amino acids of SEQ ID NO. 4 and must specifically bind to a LAT polypeptide according to SEQ ID NO. 4 (i.e., the full length LAT polypeptide). There is no teaching or suggestion of antibodies with these properties anywhere in Buday. To the extent Buday's antibody might arguably recognize a phosphorylated tyrosine in a phosphorylated LAT polypeptide, it does not recognize a sequence of at least 5 amino acids of a LAT polypeptide according to SEQ ID NO: 4 and therefore does not have the same binding specificity

required by claims 70-84.

Therefore, because Buday does not teach each element of the claims as required under 35 U.S.C. § 102, Buday does not anticipate the claims. See *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978) ("[r]jections under 35 U.S.C. §102 are proper only when the claimed subject matter is identically disclosed or described in the prior art.>").

Applicants respectfully request that in view of the above arguments, the rejection should be reconsidered and withdrawn.

Rejection of Claims 4-5, 29 and 33 Under 35 U.S.C. § 102(e) (Hirth)

Claims 4-5, 29 and 33 stand rejected under 35 U.S.C. § 102(e) over Hirth, et al., U.S. Patent 5,058,959 ("Hirth"). The Examiner asserts that the antibody of Hirth is directed against a phosphotyrosine residue and as such, because the term "portion" reads on a single amino acid, Hirth allegedly anticipates the claims.

Applicants respectfully traverse the rejection as applied to the amended and newly added claims. As discussed above, as amended, claims 61-69 require that the antibodies recognize and *specifically* bind to a LAT polypeptide according to SEQ ID NO: 4 (i.e., a full length LAT polypeptide) and must *not cross react* with non-LAT ZAP 70 or non-LAT Syk substrates (i.e., non-LAT polypeptides which are phosphorylated by ZAP 70 and/or Syk). Hirth's antibodies would non-specifically cross-react with any polypeptides comprising a phosphotyrosine, including non-LAT ZAP 70 or non-LAT Syk substrates. Additionally, Hirth neither teaches nor suggests antibodies which recognize and specifically bind to a full length LAT polypeptide according to SEQ ID NO: 4 and which are generated against a polypeptide which comprises at least about 5 amino acids of SEQ ID NO. 4 as claimed in claims 70-84. Hirth nowhere teaches or suggests antibodies with these properties.

Therefore, in view of the above arguments, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejection of Claim 38 Under 35 U.S.C. § 112, First Paragraph

Claim 38 is rejected under 35 U.S.C. § 112, first paragraph. The Office Action expressly acknowledges that the specification is enabling for an antibody that binds a portion of SEQ ID NO:4. However, the position is taken that the specification does not reasonably enable an antibody that binds to “just any 20 amino acids” of SEQ ID NO:4 because antibodies generated against 20 amino acid fragments would not recognize the folded protein and as such would not be useful in detection. The Examiner concludes that it would require undue experimentation to use the claimed invention.

Applicants respectfully submit the rejection is moot in view of the cancellation of claim 38 and traverse the rejection to the extent it would be applied against any of the newly added claims. Antibodies are routinely generated against protein fragments and are routinely used in assays which do not rely on detecting tertiary conformations of proteins. For example, it was standard in the art at the time of filing (and still is) to perform Western blots of proteins electrophoresed on polyacrylamide gels comprising 10% SDS. In such gels, the proteins are denatured and do not retain the tertiary structure of the native protein. Yet Western blots have undeniable utility in assays which rely on the detection of specific proteins (e.g., such as in diagnostic assays). Additionally, antibodies generated against LAT peptides are also able to recognize non-denatured proteins in Flow Cytometry Assays as well as in immunohistochemistry assays. Accordingly, Applicants respectfully submit that the rejection of claim 38 is improper and should be reconsidered and withdrawn.

Rejection of Claims 39-44 Under 35 U.S.C. § 112, First Paragraph

Claims 39-44 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner specifically objects to claims which recite "wherein SEQ ID NO: 4 comprises a carboxy-terminus and an amino-terminus, wherein said portion comprises at least 20 amino acids from" either the amino-terminus or carboxy-terminus. The Examiner asserts that "there is no support for antibodies that bind to at least 20 amino acids from the amino-terminal or carboxy-terminal."

Applicants respectfully submit that the rejection is moot in view of the cancellation of claim 39 and the fact that none of the newly added claims contain this language. Claim 39 has been cancelled solely to expedite the prosecution of the instant application as Applicants respectfully submit that specification clearly states at page 40 that that the present invention is not limited to specific portions of LAT for the generation of antibodies. As such, newly added claim 61 includes antibodies which recognize both N- and C-termini, as well as internal fragments of LAT and mutant forms of LAT.

In view of the above amendments and arguments, Applicants respectfully request that the rejection be reconsidered and withdrawn.

CONCLUSION

Applicants submit that the claims are allowable and that the Application is now in condition for allowance. Applicants respectfully request early favorable action by the Examiner.

Attorney Docket No. 58118 ~~RE~~ (47992) (formerly NIH-05065)
U.S.S.N.: 09/597,920
Filed: June 19, 2000.
Amendment and Remarks
Page 11 of 11

If the Examiner believes that a telephone conversation with Applicants' agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned agent of record.

April 2, 2003

By: *Dianne Rees*
Dianne M. Rees, Ph.D. (Reg. 45,281)
EDWARDS & ANGELL, LLP
PO BOX 9169
Boston, Massachusetts 02209
(617) 951-3351

Customer No: 21,874

BOS2_330849.1